

CLINICAL GUIDELINES FOR ZOHYDRO™ ER

Description: Zohydro™ ER (hydrocodone bitartate) is an oral semisynthetic opiate agonist derived from the opioid alkaloid, thebaine and is similar to other phenanthrene derivatives such as codeine. Hydrocodone extended-release capsules (Zohydro™ ER) are used to manage pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Zohydro™ ER is the first extended-release dosage form of hydrocodone and the first dosage form of hydrocodone that is not combined with an analgesic such as acetaminophen. Due to the risks of addiction, abuse, misuse and diversion with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, Zohydro™ ER should be reserved for use in patients for whom alternative treatment options are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. The product is not approved for as-needed pain relief. The recommended dose is every 12 hours. Hydrocodone extended-release capsules were FDA-approved in October 2013. Available strengths 10mg, 15mg, 20mg, 30mg, 40mg, and 50mg.

Indication: For the management of severe pain that requires daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Zohydro™ ER has significant black-box warnings.

Zohydro™ ER (hydrocodone bitartrate) Extended-Release Capsules, CII
Initial U.S. Approval: 1943

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL EXPOSURE; NEONATAL OPIOID WITHDRAWAL SYNDROME; and INTERACTION WITH ALCOHOL

See full prescribing information for complete boxed warning.

- Zohydro ER exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk before prescribing, and monitor regularly for development of these behaviors or conditions. (5.1)
- Serious, life-threatening, or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase. Instruct patients to swallow Zohydro ER whole to avoid exposure to a potentially fatal dose of hydrocodone. (5.2)
- Accidental consumption of Zohydro ER, especially in children, can result in fatal overdose of hydrocodone. (5.2)
- For patients who require opioid therapy while pregnant, be aware that infants may require treatment for neonatal opioid withdrawal syndrome. Prolonged use during pregnancy can result in life-threatening neonatal opioid withdrawal syndrome. (5.3)
- Instruct patients not to consume alcohol or any products containing alcohol while taking Zohydro ER because co-ingestion can result in fatal plasma hydrocodone levels. (5.4)

Black box warning from Official Prescribing Information

In December 2013, the Centers for Medicare and Medicaid Services (CMS) Program Integrity Group sent an alert letter to Medicare Part D plans notifying them about this product and encouraging them to consider employing utilization management strategies such as prior authorization (PA) and quantity limits to help ensure safe and appropriate utilization of Zohydro™ ER (copy attached).

Long-acting Narcotic Analgesics is a reviewed class and the DOM P&T Committee placed Zohydro™ ER on the non-preferred list when it was introduced to the market. As shown below, the current Preferred Drug List (PDL) lists specific product related and general class related step-edits and quantity limits for the non-preferred agents in this class.

ANALGESICS, NARCOTIC - LONG ACTING SmartPA			
	fentanyl patches methadone morphine ER tablets OPANA ER (oxymorphone)	AVINZA (morphine) BUTRANS (buprenorphine) CONZIP ER (tramadol) DOLOPHINE (methadone) DURAGESIC (fentanyl) EMBEDA (morphine/naltrexone) EXALGO (hydromorphone) hydromorphone ER KADIAN (morphine) MS CONTIN (morphine) morphine ER capsules NUCYNTA ER (tapentadol) oxycodone ER OXYCONTIN (oxycodone) oxymorphone ER RYZOLT (tramadol) tramadol ER ULTRAM ER (tramadol) XARTEMIS XR (oxycodone/APAP) ^{NR} ZOHYDRO ER (hydrocodone bitartrate)	SmartPA Criteria: <ul style="list-style-type: none"> • Suboxone/ Subutex concurrent therapy <ul style="list-style-type: none"> ○ Opioids are limited to a 5 day supply while on Suboxone or Subutex therapy with a maximum cumulative total of 10 days. • Avinza <ul style="list-style-type: none"> ○ 30 days of therapy with Opana ER or morphine ER in the past 6 months OR ○ 90 days completed therapy with the same agent in the past 105 days AND ○ Quantity limit of 31 tablets in 31 days • OxyContin <ul style="list-style-type: none"> ○ Documented diagnosis of cancer found in the past 2 years medical claims OR ○ Antineoplastic therapy in the past 6 months AND ○ 30 days of therapy with Kadian, Opana ER, morphine ER, Avinza or Duragesic patch in the past 6 months AND
			<ul style="list-style-type: none"> ○ Quantity limit of 62 tablets in 31 days. • Non-Preferred Criteria <ul style="list-style-type: none"> ○ 30 days of therapy with 2 different preferred agents in the past 6 months OR ○ 90 days completed therapy with the same agent in the past 105 days AND ○ Applicable <u>quantity limit</u> in 31 rolling days. <ul style="list-style-type: none"> • 31 tablets in 31 days – Exalgo ER, Ultram ER, Ryzolt, Conzip ER, • 62 tablets in 31 days – Methadone, Kadian, Morphine ER, Embeda, oxycodone ER, Opana ER, • 10 patches in 31 days – Duragesic • 4 patches in 31 days - Butrans

Recommendation:

MS-DUR recommends that DOM place additional product specific PA criteria for use of Zohydro™ ER and that the DUR Board provide input on possible additional criteria.

Possible Criteria If Recommendation Approved by Board:

The following potential criteria and areas for discussion have been identified by MS-DUR and DOM.

Age edit	Minimum age of 18 years
Quantity limit	Maximum 2 units per day, 62 tablets in 31 days (<i>similar to Methadone, Kadian, Morphine ER, Embeda, oxycodone ER, Opana ER</i>)
Diagnosis	Documented diagnosis of HIV, cancer, or sickle cell disease – <i>should we limit to specific diagnoses?</i>
Step-therapy	Prior 30 days of therapy with 2 different preferred agents in the past 6 months OR Prior 30 days therapy with Kadian, Opana ER, morphine ER, Avinza or Duragesic patch in the past 6 months (<i>similar to OxyContin</i>) OR 90 days completed therapy with Zohydro™ ER in the past 105 days (<i>allows grandfathering for beneficiaries already on therapy when implemented</i>)

Recommendation:

The DUR Board recommends that DOM adopt the product specific PA criteria for use of Zohydro™ ER identified during the discussion.

ATTACHMENT – CMS ADVISORY TO MEDICARE PART D PLANS

DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850



Center for Program Integrity

Date: December 17, 2013
To: All Medicare Part D Plan Sponsors
From: Mark Majestic, Acting Director
Medicare Program Integrity Group
Re: Alert - Zohydro™ ER

On October 25, 2013 the Food and Drug Administration (FDA) approved Zohydro™ ER (hydrocodone bitartrate), an extended-release/long-acting (ER/LA) opioid analgesic. Zohydro™ ER is the first single entity hydrocodone product approved by the FDA. Zohydro™ ER is similar to OxyContin®, in that it is a potent oral opioid analgesic that is formulated without acetaminophen (APAP). ER/LA opioid formulations, in addition to the risk of abuse and addiction associated with all opioids, carry a greater risk of overdose and death because they are easier to prepare for injection or snorting due to the higher undiluted opioid dose. As such, Zohydro™ ER is part of the FDA required Risk Evaluation and Mitigation Strategy (REMS) for Extended-Release (ER) and Long-Acting (LA) Opioids. In 2010, OxyContin® was reformulated to make the tablet more difficult to crush, break or dissolve to deter abuse by injection or snorting. Contrary to FDA recommendations, Zohydro™ ER is not in an abuse-deterrent form¹. It may therefore be preferentially sought for abuse and diversion.

We are alerting you to this information so that you can take appropriate measures regarding this product in your Part D prescription drug benefit. Zohydro™ ER has a more narrow indication than hydrocodone/APAP products and the approved product labeling includes a boxed warning regarding the risks of addiction, abuse and misuse which can lead to overdose and death. As such, Part D sponsors may wish to employ utilization management strategies such as prior authorization and quantity limits to help ensure safe and appropriate utilization.

If you need additional information about this issue, please contact the NBI MEDIC at 1-877-7SAFERX (1-877-772-3379). Any questions on this subject should be emailed to CPIMedicarePartD_Data@cms.hhs.gov.

¹ http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/202880Orig1s000SumR.pdf

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This information has not been publicly disclosed and may be privileged and confidential. It is for internal government use only and must not be disseminated, distributed, or copied to persons not authorized to receive the information. Unauthorized disclosure may result in prosecution to the full extent of the law.